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EXAMINER	
HOLBROOK, PAMELA G	

ART UNIT	PAPER NUMBER
1647	4

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/784,670	Applicant(s) ZHU ET AL.	
	Examiner Pamela G Holbrook	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) _____ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Objections

1. Claim 11 is objected to because " wherein particles of such construct range from under 20 micrometers to under 10 micometers" does not designate a range. Under 10 micrometers is encompassed by under 20 micrometers. Thus, for examination purposes, "under 20 micrometers to under 10 micometers" will be interpreted to mean under 20 micrometers and claim 11 is identical to claim 12.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites a "polymeric construct". A suitable polymeric construct is described in the specification as "one which will incorporate therein or encapsulate the selected medicament" (page 13 line 4). The precise nature of the claimed construct is unclear and is variously referred to in the specification as "aerosol particles comprising polysaccharide vesicles" (page 3, line 4), a "polymeric construct particle" (page 12, line 23) and a "gel-like structure" (page 14, line 5). Thus, in the recitation of

polymeric construct, claim 1 fails to particularly point and distinctly describe the metes and bounds of the subject matter that the applicant claims to have invented. Claims 2-14 or also rejected for depending from a rejected claim, claim 1.

Claim 8 is vague and indefinite in the recitation of "suitable anti-solvent" since it is not immediately apparent what anti-solvent means and suitability would likely vary depending on the solvent and polymer used in the method. Claims 11 and 14 are also rejected for depending from a rejected claim, claim 8.

In the recitation of "a critical pressure and temperature" claims 8 and 9 fail to particularly point out and distinctly claim the metes and bounds of the claimed invention since "critical" provides no specific information about the temperature or pressure required to achieve formation of the construct and these conditions would likely vary depending on the solvent, polysaccharide polymer or medicament used. Further when these conditions are not particulary specified in a method, standard or ambient temperature and pressure are assumed and would also qualify as "critical". Claim 12 is also rejected for depending from a rejected claim, claim 9.

Claim 9 is vague and indefinite in the recitation of "appropriate anti-solvent" since it is not immediately apparent what anti-solvent means and appropriateness would likely vary depending on the solvent and polymer used in the method. Claim 12 is also rejected for depending from a rejected claim, claim 9.

Claims 11-14 recite the limitation "particles of such construct" in further limiting claims 8-11 respectively. There is insufficient antecedent basis for this limitation in the claims.

Claims 11, 12 and 14 are vague and indefinite in the recitation of particles "under 10 or under 20 micrometers in diameter" since such language fails to establish a lower limit for particle diameter.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2 and 6 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Goosen et al. [US Patent 4689293 (Aug. 25,1987)].

Claim 1 is drawn to a polymeric construct comprising a polysaccharide polymer having a selected medicament entrapped therewithin. Claim 2 is drawn to the construct of claim 1 wherein said polymer is selected from the group consisting of

alginic acid or a salt thereof or any of a group of other polysaccharide gums and mixtures thereof.

Goosen et al. teach the encapsulation of biologically active materials in a biocompatible semi-permeable membrane, in the form of a hydrogel (column 2, last parpagraph) said capsule being formed from a polysaccharide gum most preferably the gum being the alkali metal of alginate (column 3, 3rd paragraph). Goosen et al. clearly anticipates the inventions of claims 1 and 2.

Claim 6 is drawn to the construct of claim 2 wherein said polymer is present in an amount of about 0.0000001 to about 10% by weight of said construct.

Goosen et al. teach that the outer biochemically inert but biocompatible alginate surface is a negatively charged hydrogel containing about 90% water (column 5, 1st sentence, 4th paragraph). Goosen et al. clearly anticipates the invention of claim 6.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goosen et al. [US Patent 4689293 (Aug. 25,1987)] as applied to claims 1 and 2 above in view of Mathiowitz et al. [J. Appl. Polymer Sci. (1988) 35: 755-774].

Claim 3 is drawn to the construct as defined in claim 1 (see above) wherein said medicament comprises proteins and peptides.

Goosen et al. teach the encapsulation of biologically active materials in a biocompatible semi-permeable membrane, in the form of a hydrogel (column 2, last parpagraph) said capsule being formed from a polysaccharide gum (column 3, 3rd paragraph).

Goosen et al. fail to teach a medicament comprising proteins and peptide.

Mathiowitz et al. teach the release of drugs from polyanhydride microspheres (see abstract page 755) and provide specific information about the release of the protein, insulin from said microspheres (Figures 9 and 10 page 769-770).

Thus it would have been *prima facie* obvious to one of ordinary skill in the art to combine the constructs of Goosen et al. and Mathiowitz et al. to produce a polymeric construct comprising a polysaccharide polymer construct having a selected protein or peptide medicament entrapped therein and one would have been motivated to do

so with a reasonable expectation of success, in order to facilitate the delivery of the proteins or peptides.

Further it would have been *prima facie* obvious to one of ordinary skill in the art to prepare a construct to entrap any one or all of the biologically active medicaments listed in claims 3-5 within a polysaccharide, polymeric construct and one would have been motivated to do so with a reasonable expectation of success, in order to facilitate delivery of said medicament.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goosen et al. [US Patent 4689293] as applied to claims 1 and 2 above in view of Mathiowitz et al. [J. Controlled Release (1987) 5: 13-22].

Goosen et al. teach the encapsulation of biologically active materials in a biocompatible semi-permeable membrane, in the form of a hydrogel (column 2 , last parpagraph) said capsule being formed from a polysaccharide gum (column 3, 3rd paragraph).

Goosen et al. fail to teach a method of preparing the construct of claim 1 which comprises, combining said polymer with said medicament to form a mixture; subjecting said mixture to agitation or mixing at the temperature of about 0.5 to 28° C for about 0.1 to 96 hours to form the construct.

Maithiowitz et al. teach a process of "hot melt encapsulation" in which: 1) melted polymer is mixed with a drug or protein such as insulin, 2) suspended in a non-miscible solvent 5º C above the melting point of the polymer and, 3) stirred continuously until the emulsion is stabilized (page 14, column 2, 2nd paragraph).

Thus it would have been *prima facie* obvious to one of ordinary skill in the art to combine the constructs of Goosen et al. and Mathiowitz et al. to produce a polymeric construct by combining said polysaccharide polymer with said medicament to form a mixture; subjecting said mixture to agitation or mixing at the temperature of about 0.5 to 28º C for about 0.1 to 96 hours to form the construct and one would have been motivated to do so with a reasonable expectation of success, in order to prepare particles for drug delivery.

Claims 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goosen et al. [US Patent 4689293] as applied to claims 1 and 2 above in view of Mathiowitz et al. [J. Appl. Polymer Sci (1988) 35: 755-774].

Goosen et al. teach the encapsulation of biologically active materials in a biocompatible semi-permeable membrane, in the form of a hydrogel (column 2 , last parpagraph) said capsule being formed from a polysaccharide gum (column 3, 3rd paragraph).

Goosen et al. fail to teach a method of preparing the construct of claim 1 which comprises, dissolving said polymer and said medicament in a solvent to form a solution; exposing said solution to a critical temperature and pressure while mixing with a suitable antisolvent.

Maithiowitz et al. teach a "solvent removal technique" for microsphere preparation in which: 1) polymer is dissolved in methylene chloride, 2) the drug is then suspended in the solution, mixed, dropped into silicon oil and stirred and, 3) after 1 hour petroleum ether is added and stirred for an additional hour (page 758, paragraph 3).

Thus it would have been *prima facie* obvious to one of ordinary skill in the art to combine the constructs of Goosen et al. and Mathiowitz et al. to produce a polysaccharide polymeric construct by dissolving said polysaccharide and said medicament in a solvent to form a solution; exposing said solution to a critical temperature and pressure while mixing with a suitable antisolvent and one would have been motivated to do so with a reasonable expectation of success, in order to prepare particles for drug delivery.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goosen et al. [US Patent 4689293] as applied to claims 1 and 2 above in view of Mathiowitz et al. [J. Appl. Polymer Sci (1988) 35: 755-774].

Goosen et al. teach the encapsulation of biologically active materials in a biocompatible semi-permeable membrane, in the form of a hydrogel (column 2 , last parpagraph) said capsule being formed from a polysaccharide gum (column 3, 3rd paragraph).

Goosen et al. fail to teach a method of preparing the construct of claim 1 which comprises, dispersing said polymer in a solution of said medicament to form a dispersion; subjecting said dispersion to a critical temperature and pressure while mixing with an appropriate anti-solvent to separate the construct after about 0.0001 to 24 hours.

Maithiowitz et al. teach a "solvent removal technique" for microsphere preparation in which: 1) polymer is dissolved in methylene chloride, 2) the drug is then suspended in the solution, mixed, dropped into silicon oil and stirred and, 3) after 1 hour petroleum ether is added and stirred for an additional hour (page 758, paragraph 3).

Thus it would have been *prima facie* obvious to one of ordinary skill in the art to combine the constructs of Goosen et al. and Mathiowitz et al. to produce a polysaccharide polymeric construct by dispersing said polymer in a solution of said medicament to form a dispersion; subjecting said dispersion to a critical temperature and pressure while mixing with an appropriate anti-solvent to separate the construct

after about 0.0001 to 24 hours and one would have been motivated to do so with a reasonable expectation of success, in order to prepare particles for drug delivery.

Claims 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goosen et al. [US Patent 4689293] as applied to claims 1 and 2 above in view of Mathiowitz et al. [J. Appl. Polymer Sci (1992) 45: 125-134].

Goosen et al. teach the encapsulation of biologically active materials in a biocompatible semi-permeable membrane, in the form of a hydrogel (column 2, last parpagraph) said capsule being formed from a polysaccharide gum (column 3, 3rd paragraph).

Goosen et al. fail to teach a method of preparing the construct of claim 1 which comprises, dissolving said polymer in a solution of said medicament to form a polymer solution and drying said polymer solution as a spray for about 0.1 to about 8 hours.

Maithiowitz et al. teach a "spray drying technique" for microencapsulation in which: 1) polymer is dissolved in methylene chloride 2) soluble drugs are codissolved in the polymer solution and 3) the solution is then spray-dryed (page 126, 2nd column, 1st paragraph).

Thus it would have been *prima facie* obvious to one of ordinary skill in the art to combine the constructs of Goosen et al. and Mathiowitz et al. to produce a polysaccharide polymeric construct by dissolving said polysaccharide in a solution of said medicament to form a polymer solution and drying said polymer solution as a spray for about 0.1 to about 8 hours and one would have been motivated to do so with a reasonable expectation of success, in order to prepare particles of the construct for drug delivery.

Claims 11 and 12 are rejected under 35 U.S.C. 103(b) as being unpatentable over Goosen et al. [US Patent 4689293] as applied to claims 1 and 2 above in view of Steiner et al. [US Patent 6071497 (Jun. 6, 2000)].

Goosen et al. teach the encapsulation of biologically active materials in a biocompatible semi-permeable membrane, in the form of a hydrogel (column 2, last parpagraph) said capsule being formed from a polysaccharide gum (column 3, 3rd paragraph).

Goosen et al. fail to teach a method of preparing the construct of claim 1 wherein particles of such construct are under 20 micrometers in diameter

Steiner et al. teach drug delivery to the pulmonary system by encapsulation in microparticles formed from biodegradable synthetic materials or natural polymers

including alginate and other polysaccharides (column 3, line 34) having a size range between 0.5 and 10 microns (see abstract).

Thus it would have been *prima facie* obvious to one of ordinary skill in the art to combine the constructs of Goosen et al. and Steiner et al. to produce a polysaccharide polymeric construct wherein particles of such construct are under 20 micrometers in diameter and one would have been motivated to do so with a reasonable expectation of success, in order to achieve pulmonary drug delivery.

Claims 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steiner et al. [US Patent 6071497 (Jun. 6, 2000)] above in view Edwards et al. [US Patent 5874064 (Feb. 23, 1999)].

Steiner et al. teach drug delivery to the pulmonary system by encapsulation in microparticles formed from biodegradable synthetic materials or natural polymers including alginate and other polysaccharides (column 3, line 34) having a size range between 0.5 and 10 microns (see abstract).

Steiner et al. do not teach particles about 10 micrometers to about 20 micormeters in diameter (claim 13) or ranging from under 10 micrometers to about 20 micrometers in diameter (claim 14)

Edwards et al. teach improved light particles for drug delivery to the pulmonary system made of biodegradable polymers with a mass mean diameter of 5 to 30 micometers.

Thus it would have been *prima facie* obvious to one of ordinary skill in the art to combine the constructs of Steiner et al. and Edwards et al. to produce particles about 10 micormeters to about 20 micormeters in diameter or ranging from under 10 micometers to about 20 micrometers in diameter and one would have been motivated to do so with a reasonable expectation of success, in order to achieve pulmonary drug delivery.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pamela Holbrook whose telephone number is (703) 306-3221, Mon.- Fri. 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564.

The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

December 18, 2001

Gary L. Kunz

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